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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,152	06/20/2003	Sharon A. Baughman	P1775R1D1	5622

9157 7590 08/09/2006

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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 08/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/600,152	BAUGHMAN ET AL.	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29,31-37,86-97,99 and 101* is/are pending in the application.

4a) Of the above claim(s) *34-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29,31-33,37,86-97,99 and 101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/05 6/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicants' election of Group I in the reply filed on 5/24/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. The amendment filed 5/24/2006 is acknowledged. Claims 30, 98, 100 and 102-105 were canceled.

Claims 1-29, 31-37, 86-97, 99 and 101 are pending. Claims 34-36, drawn to non-elected inventions, are withdrawn from consideration. Claims 1-29, 31-33, 37, 86-97, and 101 are examined on the merits. Applicants' election of species of chemotherapeutic agent, which is paclitaxel, is acknowledged.

Claim Rejections - 35 USC § 112

3. Claims 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 10 are indefinite because they contain improper Markush language: "selected from the group consisting essentially of". This rejection would be overcome by amending to recite: "selected from the group consisting of".

4. Claims 1-22, 27-29, 31-33, and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating cancer characterized by overexpression of ErbB2 receptor, does not reasonably provide enablement for methods of treating a human patient susceptible to or diagnosed with a disorder characterized by overexpression of ErbB2 receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The claims are broadly drawn to methods having the intended use of treating patients susceptible to or diagnosed with a disorder characterized by overexpression of ErbB2 receptor. In one aspect, the claims encompass methods of prevention of diseases characterized by overexpression of ErbB2 receptors. In another aspect, the claims are broadly drawn to methods for treatment of any and all diseases characterized by overexpression of ErbB2 receptor.

The specification provides working examples that demonstrate regimens for delivery of anti-ErbB2 antibodies. The examples are concern specifically the delivery of HERCEPTIN®, which is the humanized 4D5 antibody that binds ErbB2, and specifically concern the treatment of patients with histologically confirmed ErbB2 over-expressing metastatic breast cancer. Thus,

the guidance provided by the specification is not commensurate in scope with the scope of the intended use of the claimed methods, which are broadly drawn to treating or preventing diseases characterized by overexpressing ErbB2. The specification does prophetically contemplate other diseases and disorders such as various benign and malignant tumors, and other disorders such as neuronal, glial, astocytal, hypothalmic and other glandular, macrophagal, epithelial, stromal and blastocoelic disorders, and inflammatory angiogenic and immunologic disorders. However, no nexus is provided between the treatment of metastatic breast cancer and any other disorder, and it is not clear that the specific dosages or protocols recited in the claims would be useful in treating any other the other contemplated disorders.

Furthermore, the claims read on methods of prevention of disease. Because the antibody used in the claimed methods is an anti-ErbB2 antibody, this implies that overexpression of ErbB2 in some tissue at some point before development of malignant disease could be used as an indicator that treatment with an anti-ErbB2 antibody would be beneficial. However, the specification provides no guidance for this concept. Additionally, Rohan (Rohan, T.E., et al., Journal of the National Cancer Institute, 90(17): 1262-1269, 1998) teaches that c-erbB2 over expression does not appear to be associated with an increased risk of progression in breast cancer. Therefore, it does not appear that it is predictable that treatment with an anti-ErbB2 antibody would be useful in the prevention of malignant breast cancer, for example.

Given the breadth of the claims and the narrow scope of the guidance provided by the specification, further experimentation would have be undertaken by one of skill in the art to determine if treatment with an anti-ErbB2 antibody would be useful for the treatment of diseases other than cancers that overexpress ErbB2, and also if treatment with an anti-ErbB2 antibody

would be useful for the prevention of any and all diseases that overexpress ErbB2. This further experimentation would be undue experimentation because there is no guidance provided in the specification concerning the applicability of the specific dosages recited in the claims and efficacy of anti-ErbB2 antibody administration with diseases other than metastatic breast cancer. The specification and the prior art fail to teach any model systems that one could use to test the hypothesis that an anti-ErbB2 antibody could be used to treat diseases other than cancers that overexpress ErbB2. Likewise, the specification and the prior art fail to teach any model systems that could be used to test the hypothesis that an anti-ErbB2 antibody could be used to prevent a disease characterized overexpression of ErbB2. Therefore, the specification fails to enable the full scope of the intended use of claimed methods.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-7, 9, 11-13, 23-27, 31-33, 86-97, 99, and 101 are rejected under 35 U.S.C. 102(e) as being anticipated by Sliwkowski (US 6,949,245; issued Sep. 27, 2005; effective filing date June 25, 1999).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C.

102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Independent claim 1 is drawn to a method for treatment of a human patient susceptible to or diagnosed with a disorder characterized by overexpression of ErbB2 receptor, comprising administering an effective mount of an anti-ErbB2 antibody to the human patient, comprising administering to the patient an initial dose of at least approximately 5 mg/kg of the anti-ErbB2 antibody and administering to the patient a plurality of subsequent doses of the antibody in an amount that is approximately the same or less than the initial dose and further comprising administering an effective amount of a chemotherapeutic agent. Independent claim 86 is drawn to a method of treating cancer in a human comprising administering a first dose followed by at least one subsequent does, wherein the first and second subsequent doses are separated in time by at least about 2 weeks and further comprising administering an effective amount of a chemotherapeutic agent. Independent claim 101 is drawn to a method of treating cancer in a human patient comprising administering an effective amount of an anti-ErbB2 antibody to the patient, comprising administering to the patient an initial dose of at least approximately 5 mg/kg of the antibody and administering a plurality of subsequent doses of the antibody in an amount that is approximately the same or less than the initial dose and further comprising administering an effective amount of a chemotherapeutic agent.

Sliwkowski teaches a method of treating cancer comprising administering an anti-ErbB2 antibody at least one dose of between 0.1 mg/kg and 15mg/kg (see claim 17, and also see column

48, lines 19-51). The doses may be separated by one week or by about 3 weeks. Sliwkowski also teaches that the antibody may be administered in combination with a chemotherapeutic agent such as paclitaxel, which is a taxoid (see column 20, lines 7-9, column 47, lines 17-23, and lines 48-51), and that synergy might occur leading to a lowering of the dosages (see column 48 lines 15-18). Sliwkowski also teaches intravenous and subcutaneous administration. Sliwkowski teaches treatment of cancer, for example cancers such as breast cancer, metastatic breast cancer, lung cancer, colorectal cancer, ovarian cancer (see column 45, lines 27-43, and claims 21 and 22). The antibody of Sliwkowski binds to the extracellular domain of the ErbB2 receptor (see Figure 1B). Sliwkowski teaches that the progress of therapy is easily monitored by conventional techniques and assays (column 48, lines 50-51). The first and second doses may be the same or the subsequent dose may be less than the initial dose (see column 48 lines 44-45). Thus, Sliwkowski teaches the methods as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-3, 5, 11, 17, 18, 22-29, 31, 32, 86-90, 92, 99, and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watanabe (Watanabe, T. et al., Proceedings of ASCO, 17: Abstract #702, 1998; cited in the IDS) in view of Seidman (Seidman, A.D. et al. Seminars in Oncology, 22(5): 108-116, 1995) and further in view of Baselga (Baselga, J. et al., Proceedings of the American Association for Cancer Research, 35: 380, Abstract #2262, 1994).

Watanabe teaches a method of treating metastatic breast cancer patients that express ErbB2 (Her2), comprising administering a dose of 8mg/ml and subsequent doses of 8mg/ml, where the initial and subsequent doses are separated in time by 3 weeks, and where the subsequent doses are separated from each other by 1 week. Tumor response is observed in five patients. Watanabe fails to teach a method further comprising the administration of paclitaxel.

However, Seidman teaches that paclitaxel is used to treat breast cancer both as a single-agent and in combination therapies. Seidman teaches that in vitro experiments indicate that paclitaxel and anti-Her-2 antibodies may have a synergistic effect (see page 108, abstract and 1st

col., and page 112, 1st and 2nd col., bridging paragraph). Furthermore, Baselga teaches that administration of paclitaxel in combination with humanized 4D5 anti-ErbB2 antibody is synergistic in a human breast cancer xenograft model, where the combination results in 93% inhibition of tumor growth versus 35% inhibition of tumor growth in animals receiving only paclitaxel or only the antibody. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have altered the method of Watanabe to include the coadministration of paclitaxel, which is taught by Seidman to be a treatment for breast cancer. One would have been motivated to have used this combination of treatments because the experimental results of Baselga demonstrate synergy between paclitaxel and anti-ErbB2 antibody therapies.

7. Claims 1, 5, 22-29, 31, 32, and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Baselga-1994 (Baselga, J. et al Breast Cancer Research and Treatment, 32(suppl): page 30, Abstract #5, 1994) or Baselga-1996 (Baselga, J. et al., Journal of Clinical Oncology, 14(3): 737-744, 1996; cited in the IDS) in view of Seidman (Seidman, A.D. et al. Seminars in Oncology, 22(5): 108-116, 1995) and further in view of Baselga (Baselga, J. et al., Proceedings of the American Association for Cancer Research, 35: 380, Abstract #2262, 1994).

Baselga-1994 teaches a method of treating metastatic breast cancer patients that overexpress ErbB2 (Her2), comprising administering a dose of 250 mg intravenously over 90 minutes and subsequent doses of 100 mg weekly. Baselga-1996 teaches a method of treating metastatic breast cancer patients that overexpress ErbB2 (Her2), comprising administering a dose of 250 mg intravenously over 90 minutes and subsequent doses of 100 mg weekly. The doses of

Baselga-1994 and Baselga-1996 are not expressed as mg/kg. However, these doses encompass doses such as 5mg/kg as an initial does, because 250mg given to a 50kg patient would result in a 5mg/kg dose. Tumor responses were observed. Neither Baselga-1994 nor Baselga-1996 teaches a method further comprising the administration of paclitaxel.

However, Seidman teaches that paclitaxel is used to treat breast cancer both as a single-agent and in combination therapies. Seidman teaches that in vitro experiments indicate that paclitaxel and anti-Her-2 antibodies may have a synergistic effect (see page 108, abstract and 1st col., and page 112, 1st and 2nd col., bridging paragraph). Furthermore, Baselga teaches that administration of paclitaxel in combination with humanized 4D5 anti-ErbB2 antibody is synergistic in a human breast cancer xenograft model, where the combination results in 93% inhibition of tumor growth versus 35% inhibition of tumor growth in animals receiving only paclitaxel or only the antibody. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have altered the method of either Baselga-1994 or Baselga-1996 to include the coadministration of paclitaxel, which is taught by Seidman to be a treatment for breast cancer. One would have been motivated to have used this combination of treatments because the experimental results of Baselga demonstrate synergy between paclitaxel and anti-ErbB2 antibody therapies.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The

examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
August 4, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER